Does nonsense DNA speak its own dialect?

When geneticists first began to decipher the DNA code, they naturally focused on genes. That's where the action is, they thought. After all, genes specify the amino acids that make up proteins, the molecules required for life.

That focus neglects some 90 percent of the DNA in a cell.

DNA exists in the cell nucleus as long strands of paired nucleotides, or base pairs. Genes occupy particular regions of these DNA strands, called chromosomes. In a gene, each set of three nucleotides "spells" a particular amino acid. Taken together, these sets code for a particular protein.

Stretches of seemingly meaningless DNA separate genes. Gibberish can also lie between coded regions within a gene. Long ignored as "junk," this noncoding DNA nevertheless carries its own message, says Michael Simons, a molecular biologist at Harvard Medical School in Boston. He and his colleagues, working with Rosario N. Mantegna and other physicists from Boston University, have found languagelike properties in this junk.

The scientists applied two linguistics tests to genetic material from a variety of simple and complex organisms. That material included 37 DNA sequences containing at least 50,000 base pairs each, as well as two shorter sequences and one with 2.2 million base pairs. Where possible, they evaluated both coding and noncoding regions.

Coding regions are just that: codes, not languages, the Boston researchers report in the Dec. 5 PHYSICAL REVIEW LETTERS. One mistake, and the code will be misread, explains H. Eugene Stanley, part of the team's Boston University contingent. In contrast, because of what linguists call redundancy, the noncoding regions — like languages — can contain a mistake and still be understood.

Also, the frequency with which various three-, four-, five-, six-, seven-, and eight-base pair patterns appear in noncoding regions varies just as the frequency of words in a language does, the group reports. If the most common word (or pattern) occurs 10,000 times, for example, then the 10th most common one appears 1,000 times and the 100th one appears just 100 times, Stanley explains. The nucleotide threesomes in genes do not occur with such frequencies.

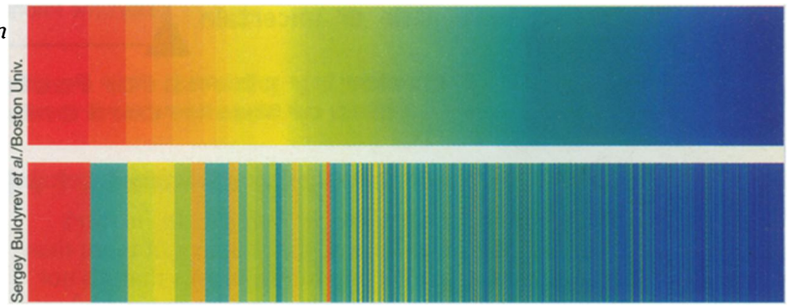
Molecular biologists had already begun to recognize differences between coding and noncoding DNA and had used these differences to find genes along unfamiliar lengths of DNA, comments Andrzej K. Konopka, a mathematical biologist at BioLingua Research, a nonprofit research group based in Frederick, Md. "[This report] is basically a confirmation of what's been known for a while," he notes. Nevertheless, he compliments the group's approach.

But Stanley asserts this work is the first to demonstrate that noncoding DNA sequences represent a structured language fundamentally unlike the coding in genes. "That's quite different from what people had thought," he says.

Some geneticists suggest this language may help place certain genes close to others. Others think noncoding regions are where chromosomes break and reconnect during recombination. But until researchers can translate this newfound language, those ideas are just speculations, Stanley notes.

Indeed, more scientists need convincing that noncoding DNA really does have a language. But that criticism doesn't faze this group. No matter what, says Harvard collaborator Ary L. Goldberger, "[the work] is going to force people to think about gene structure in ways we haven't before."

— *E. Pennisi*



In noncoding DNA, as in human language, "words" — represented as wavelengths of light — decrease in frequency in a systematic way, creating a spectrum (top). In coding regions, however, that system breaks down, with spectral colors becoming jumbled (bottom).

Bone marrow transplants: Upping the odds

For years, bone marrow transplants have tantalized researchers with the promise of a cure for potentially fatal diseases such as leukemia. However, finding a donor with an immune system that closely matches the recipient's has proved a major stumbling block.

Now, researchers have developed a method that may improve the chances of people with leukemia receiving bone marrow transplants from unmatched donors. By transplanting "megadoses" of bone marrow, sometimes as much as 10 times the amount currently used, researchers have found they can reduce the effect of donor-recipient incompatibility.

"Such doses appear to be effective because they give donor cells an edge in their competition with recipient cells, thus minimizing the risk of rejection," says Yair Reisner, a biophysicist at the Weizmann Institute of Science in Rehovot, Israel, who developed the new technique with Massimo F. Martelli, a physician at the University of Perugia in Italy.

Reisner, Martelli, and their colleagues report their findings in the Dec. 1 BLOOD.

A transplant patient receives powerful drugs and radiation therapy to wipe out his or her immune system and diseased bone marrow. The patient then receives healthy bone marrow from a donor. If the transplant takes, the donated marrow will produce new red blood cells, platelets, and white blood cells. Even with a good match, though, transplants can cause severe complications and are done only as a last resort.

Martelli and Reisner treated 17 patients in terminal stages of leukemia with megadoses of bone marrow from unmatched donors. Six of the patients lived for 3 to 16 months after receiving treatment.

To obtain such large amounts of marrow, the researchers give donors hormonal drugs called cytokines to increase the production of blood stem cells, which give rise to all types of red and white blood cells. Stem cells move from the bones into the blood, where the scientists collect 7 to 10 times as many as they normally do when taking marrow directly from the bones.

The researchers then treat the extracted marrow to eliminate T lymphocytes, white blood cells that would otherwise attack the recipient's tissues and cause graft-versus-host disease. The leukemia patients in the study, who had previously undergone drug and radiation therapy, received transfusions of this treated bone marrow.

"By eliminating the need for a very close donor-recipient match," says Reisner, "we hope this new approach will make bone marrow transplants available to all people with leukemia in need of treatment."

However, even if further studies support the effectiveness of this approach, it will take some time before it becomes widely available, he adds.

— *A.C. Brooks*